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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,704	03/22/2004	Margaret A. Wheatley	DRE-0144	8721

7590 01/29/2007

Licata & Tyrrell P.C.
66 East Main Street
Marlton, NJ 08053

EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	PAPER NUMBER
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/805,704	WHEATLEY ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/9/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3 – 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger *et al.* (US 5,585,112).

Unger discloses the use of gas-filled liposomes for therapeutic delivery of drugs that can be linked to the inside or outside wall of a microsphere, encapsulated or located in the internal microsphere void, as well as the incorporation of genetic or bioactive materials into the membrane. The bioactive materials, such as DNA may be used in the treatment of many diseases, such as cancer and malignant melanoma. The nanospheres or microspheres are particularly effective at accumulating into diseased tissue (column 31, lines 49+; column 32, lines 66+; column 35). Ultrasound may be used to rupture a gaseous precursor-filled liposome thus releasing a prodrug that has been incorporated therein, and also may cause an increase in the rate of chemical cleavage and release of the active drug (column 37, lines 52+). The administration embodiments of the microspheres or nanospheres to a patient are disclosed (column 24, lines 9 – 17). Large liposomes, e.g. between 1 and 10 microns in size, are confined to the intravascular space until cleared by phagocytic elements. For passage to cells

beyond the cells beyond the sinusoids, smaller liposomes, e.g. less than 300 nanometers in size, may be utilized (column 27, lines 13 – 20). It is noted that the instant claims 3 – 5, 10, and 11 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See *In re Thorpe*, 777 F.2d 695, 698, 277 USPQ 964, 966 (Fed Cir. 1985). See also MPEP 2113.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 4, 6, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheatley *et al.* (US 5,955,143) in view of Lamprechte (*International Journal of Pharmaceutics*, 2000, 196, p. 177 – 182).

Wheatley discloses hollow polymer microcapsules made by the method of dissolving a film-forming polymer (i.e. such as poly-lactic-co-glycolic acid, PLGA) in a volatile non-aqueous solvent, dispersing into the polymer solution a volatilizable solid core material (i.e. a sublimable substance) (abstract and claim 1). The particulate solid core material suspended in the polymer solution may be mixed with a second solution and emulsified, followed by evaporation of the first non-aqueous liquid to effect formation of the polymer microcapsules containing encapsulated solid core material (column 8, lines 25 – 40). The polymer microcapsules may be dispersed in an aqueous medium (e.g. water containing a small amount of surfactant), disaggregated to separate any aggregates, e. g. by sonication of the suspension, and thereafter subjecting the

aqueous suspension to freeze drying to remove the water and to volatilize and remove the solid core material from the polymer microcapsules (column 10, lines 40 – 47). Gases may be incorporated into the hollow microspheres, and the gas-filled polymer microspheres may be used as contrast agents in medical imaging (column 11, line 41). The microspheres may comprise a pharmaceutically active material and may be utilized in therapeutic applications as a delivery vehicle for delivering such active materials to a target locus in a patient (column 12, lines 29 – 45).

Wheatley fails to specifically teach two separate emulsion steps, and the methods of Wheatley produce microcapsules, rather than nanocapsules and microcapsules.

Lamprechte teaches the preparation of nanoparticles as an improved colloidal carrier system, wherein BSA was used as a model drug to be carried (abstract). Nanoparticles were produced by using the multiple emulsion (w/o/w) technique previously applied to the preparation of both micro- and nano-particles. The use of a homogenizer in the two-step emulsification process reduced considerably the size of the dispersed droplets. The model drug, BSA dissolved in water, was emulsified by stirring in methylene chloride containing the polymer (PLGA and PCL). This w/o emulsion was thereafter poured into an aqueous solution of polyvinylalchohol (PVA) (i.e. surfactant) and homogenized in a homogenizer. The methylene chloride was removed under reduced pressure, the polymer precipitated and the nanoparticles were washed twice before lyophilization (page 178).

Lamprechte fails to teach that the use of ammonium carbonate at the core of the nanoparticles.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to alter the synthetic methods of Wheatley to include two emulsion steps in the preparation of the microcapsules / nanocapsules to be used as drug delivery devices because Lamprechte teaches that the double emulsion technique is the most appropriate method to encapsulate hydrophilic drugs and proteins within microparticles (page 178). One would have been motivated to prepare nanocapsules of PLGA polymer for drug delivery devices, rather than microcapsules, because Lamprechte also specifically teaches the benefit of using nanoparticles in drug delivery systems because their small size allows them to permeate biological barriers (page 178).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER